Multiple primary cancers (continued)

Follow the online instructions to estimate a claimant's total PC from two or more primary cancers (Figure 11).

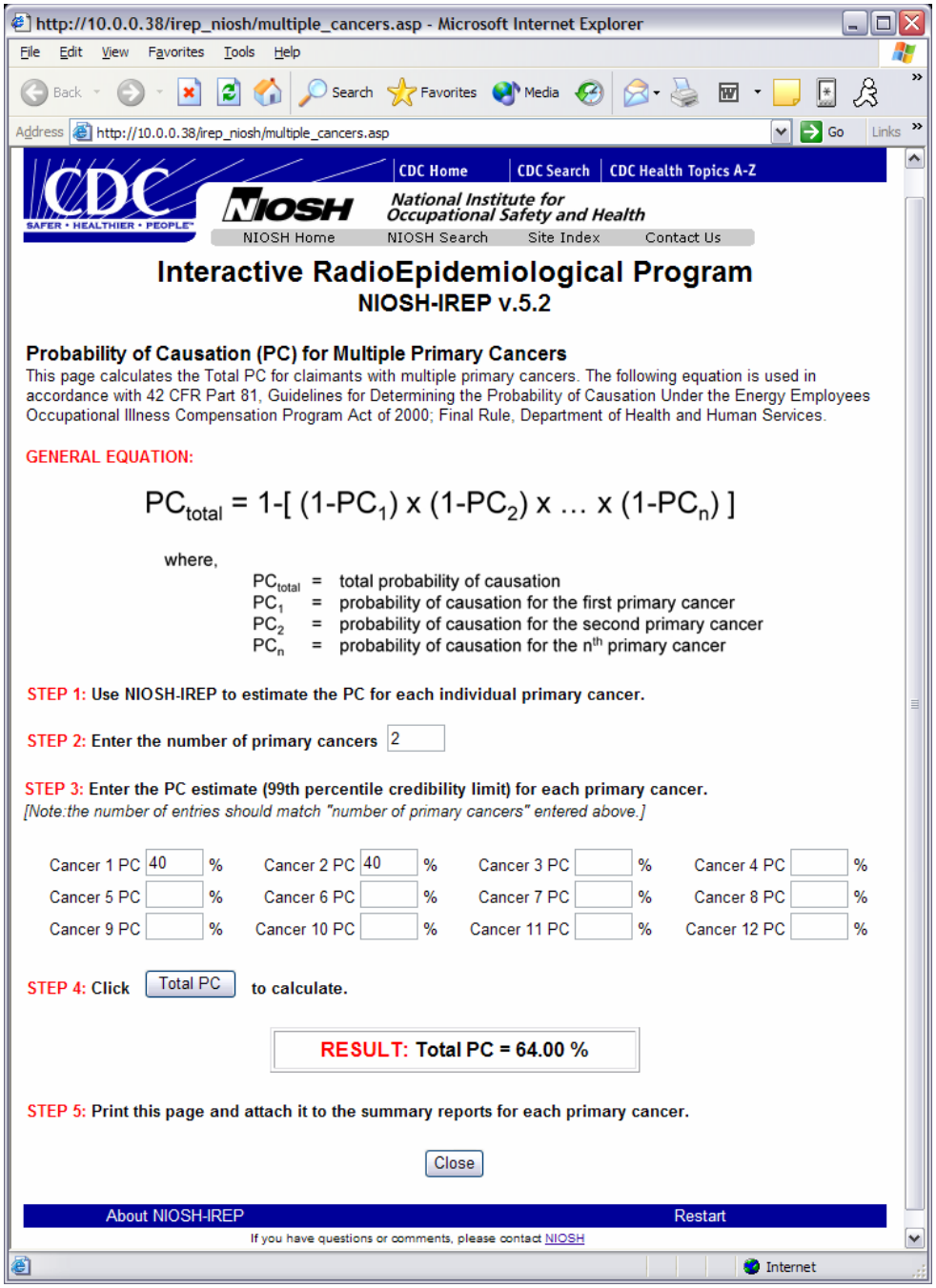

Figure 11. Multiple Primary Cancer screen

B. Alternate cancer models for a given primary cancer

In certain cases, a primary cancer will be known but more than one IREP cancer model will need to be considered. For example, certain types of leukemia will require multiple runs. For a complete listing of primary cancer sites requiring multiple runs, see Table 4 of "Cancer models to be used in calculating probability of causation" in the NIOSH-IREP Technical Documentation, which can be accessed online via the OCAS web site.

NIOSH-IREP should be run with each alternate cancer model. Use the highest resulting probability of causation at the upper 99% credibility limit to determine the claim.

C. Unknown primary cancer site

If the primary cancer site is unknown and the cancer is identified only by a secondary site or sites, multiple runs will be performed (refer to Table 7, "Primary cancers for which probability of causation is to be calculated, if only a secondary cancer site is known" in the NIOSH-IREP Technical Documentation).

NIOSH-IREP should be run with each alternate cancer model. Use the highest resulting probability of causation at the upper 99% credibility limit to determine the claim.

D. Skin cancer, if more than one ethnic origin

Claimants may have selected more than one category for “ethnic origin.” Ethnicity applies only to skin cancers (ICD-9 codes 172, 173). If more than one ethnic category has been selected, it is necessary to run each separately.

NIOSH-IREP should be run with each selected ethnic category. Use the highest resulting probability of causation at the upper 99% credibility limit to determine the claim.

E. Conflicting primary cancer sites

Multiple calculations will be required if medical records are in conflict regarding the correct site of the primary cancer, and DOL sent the claim to NIOSH listing two or more possible primary sites, even though there is only one cancer. This is expected to be a rare occurrence.

NIOSH-IREP should be run with each alternate cancer model. Use the highest resulting probability of causation at the upper 99% credibility limit to determine the claim.

4.0 TECHNICAL ASSISTANCE

Technical information about NIOSH-IREP may be obtained, and comments about NIOSH-IREP may be made, by contacting the NIOSH Office of Compensation Analysis and Support (OCAS) by e-mail at ocas@cdc.gov, or by mail at:

National Institute for Occupational Safety and Health
Office of Compensation Analysis and Support
4676 Columbia Pkwy, MS-R45
Cincinnati, OH 45226

DOL staff requiring immediate technical assistance may call the OCAS office at (513) 841-4498.

5.0 INPUT FILE TEMPLATE

The input files produced by NIOSH are in Microsoft Excel format. These input files should not be modified by DOL. A screenshot of an example input file has been provided (Figure 12) for informational purposes.

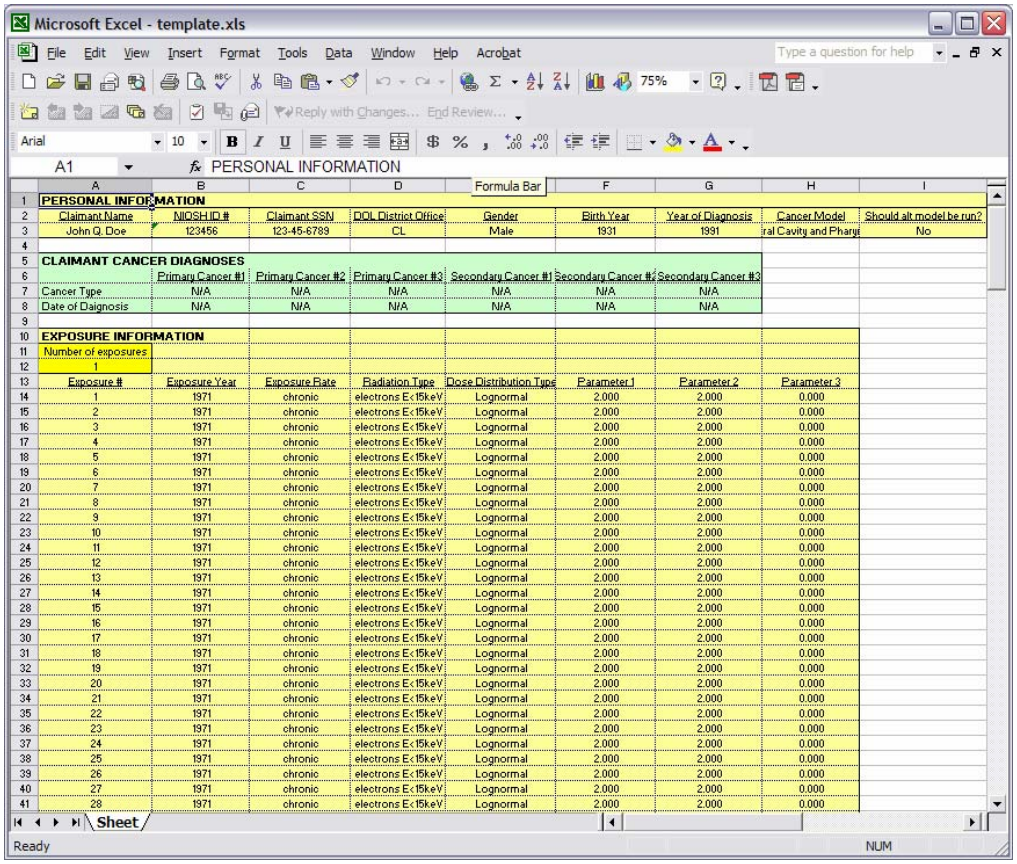

Figure 12. Screenshot of an example input file

6.0 GLOSSARY[1]

Absorbed dose: The energy deposited by *ionizing radiation* per unit mass of tissue irradiated. It can be expressed in units of *gray (Gy)* or *rad*, where 1 Gy = 100 *rad*.

Activity: The rate of transformation (or disintegration or decay) of a radioactive material. It can be expressed in units of *becquerel (Bq)* or *curie (Ci)*.

Acute dose: A *radiation dose* received by a person over a short period of time (less than one day.) A *dose* is also considered acute if it was delivered at a rate greater than 0.006 Gy per hour averaged over the first few hours.

Alpha particle: A particle emitted from a decay of certain heavy radionuclides. It has a short range and can be stopped by a sheet of paper or the outer dead layer of skin. Alpha particles constitute a health hazard only when alpha-emitting radionuclides are deposited in tissues following ingestion or inhalation.

Background radiation: Radiation emitted by natural sources such as cosmic radiation or radionuclides occurring naturally in soil, food, water or air.

Baseline cancer risk: The risk of cancer in the general population from causes other than exposure to the investigated agent (for example, the source of radiation.)

Becquerel (Bq): The unit of *activity* equal to one disintegration per second.

Beta particle: A particle emitted from a decay of certain radionuclides. It has a short range but can penetrate the dead layer of skin to produce a skin *dose*.

Carcinogen: Any substance or agent that can cause cancer.

Centi-sievert (cSv): An *equivalent dose* equal to 0.01 Sv or 1 *rem*.

[1] Words appearing in *italicized* text are also defined in the glossary.

Chronic dose: *Radiation dose* received by a person over a long period of time (more than one day.) A *dose* is also considered chronic if it was delivered at a rate lower than 0.006 Gy per hour for more than one day.

Cohort: A group of individuals sharing one or more characteristics.

Confidence interval (CI): A range of values around a mean, proportion, or rate that serves as an estimate of *uncertainty*. The upper and lower values of a confidence interval are called the confidence limits.

Confounder: A factor that distorts or masks the true effect of a given exposure in an epidemiologic study.

Covered employee: An individual who is or was an employee of DOE, a DOE contractor or subcontractor, or an atomic weapons employer.

Curie (Ci): A measure of the amount of *radioactivity* in a material. One curie is equal to 37 billion disintegrations per second.

Dose (or radiation dose): A general term representing either *absorbed dose* or *equivalent dose*.

Dose and dose-rate effectiveness factor (DDREF): A mathematical factor that takes into account that the response per unit *dose* at low *doses* and low *dose* rates may be different from the response per unit *dose* at high *doses* and high *dose* rates.

Dose reconstruction (DR): Research and analysis leading to a quantitative estimate of radiation exposure, particularly when radiation monitoring data are unavailable, incomplete, or unreliable.

Dose-response relationship: A relationship in which a change in the amount, intensity, or duration of an exposure is associated with either an increase or decrease in risk of a specified health outcome.

EEOICPA: The Energy Employees Occupational Illness Compensation Program Act of 2000, Public Law 106-398, as amended.

Electron volt (eV): The customary unit of energy for all *ionizing radiations*.

Epidemiology: The study of factors that affect health and disease in populations.

Equivalent dose: A measure of biological damage caused by exposure to radiation, expressed in units of *rem* or *sievert (Sv)*, where 1 Sv = 100 *rem*.

Erg: A unit for measuring energy.

Excess relative risk (ERR): The risk due to exposure to radiation in excess of the baseline risk, divided by the baseline risk. ERR is the same as the *relative risk (RR)* minus one.

External dose: The *dose* from radiation sources located outside the body.

Gamma rays (or gamma radiation): Electromagnetic radiation emitted from a decay of certain radionuclides. It can be very penetrating, producing a *radiation dose* throughout the whole body.

Gray (Gy): The special name for the *SI* unit of *absorbed dose*. 1 Gy = 100 *rad*.

Health physics: The science of radiation protection to reduce or prevent radiation exposure. Health physicists at *OCAS* specialize in quantifying past radiation exposures (i.e., *dose reconstruction*) in order to evaluate their health effects.

Healthy worker effect: A phenomenon in which fewer deaths or reportable illnesses (cancers, for example) are observed among workers in a given industry compared with the general population, even though the workers under study may be more exposed to hazardous substances (*ionizing radiation*, for example) than the general population. This counterintuitive effect is often attributed, in part, to the fact that chronically ill or disabled persons are less likely to be employed than "healthy" persons. Thus, a *cohort* of workers – absent that less robust segment of the population – may be more resistant to disease than the population as a whole.

Internal dose: The *dose* from radioactive materials that have been absorbed, ingested, or inhaled into the body.

Inverse dose-rate effect: A phenomenon in which a given *dose* delivered chronically or in multiple fractions results in a greater biological response than the same *dose* delivered acutely.

Ionizing radiation: Particles or rays emitted from radioactive materials. If ionization is produced in a cell, the ions may damage the cell and the affected cells may become cancerous.

Milli-sievert (mSv): An *equivalent dose* equal to 0.001 *sievert (Sv)*.

Missed dose: A *radiation dose* that was received by an individual, but that was not detected by monitory methods nor recorded.

Monte Carlo simulation: A computerized method for estimating the statistical *uncertainty* of a *risk model*. Repeated samples are taken from special probability distribution functions and the *probability of causation (PC)* is calculated for each set of samples. The upper 99th percentile of the distribution of estimated PC values (*upper 99 percent credibility limit*) is used to determine eligibility for compensation under *EEOICPA*.

Neutron: An uncharged particle of radiation produced from certain nuclear reactions. It can be very penetrating, producing a *radiation dose* throughout the whole body.

NIOSH: The National Institute for Occupational Safety and Health, part of the Centers for Disease Control and Prevention, United States Department of Health and Human Services.

Non-radiogenic cancer: A type of cancer that the Department of Health and Human Services has found not to be related to radiation.

OCAS: The Office of Compensation Analysis and Support, an Office of *NIOSH* located in Cincinnati and created to fulfill *NIOSH's* responsibilities under *EEOICPA*.

Odds ratio (OR): The ratio of the odds of disease among the exposed compared with the odds of disease among the unexposed. Under certain conditions, the odds ratio may be used as an estimate of the *relative risk*.

Organ dose: A general term representing either *absorbed dose* or *equivalent dose* received by a particular organ or tissue.

Photon: Electromagnetic radiation emitted from one of several possible sources. Photons originating from radioactive decay are called gammas or *gamma rays*.

Primary cancer: A cancer defined by the original organ site at which the cancer occurred, prior to any spread (metastasis) to other sites in the body.

Probability of causation (PC): The probability or likelihood that a cancer was caused by radiation exposure incurred by a *covered employee* while in the performance of duty. A PC of 50% or greater means that the claimant's cancer was, as least as likely as not, induced by occupational radiation exposure.

Rad: A unit of *absorbed dose*. 100 rad equals one *gray* (1 Gy).

Radiation dose: See *dose*.

Radiation effectiveness factor (REF): A mathematical factor, similar to *relative biological effectiveness (RBE)*, used to account for the fact that different types of radiation are more effective at producing an outcome (such as cancer) than others.

Radioactivity: The process or characteristic of an unstable atomic nucleus to spontaneously transform with the emission of energy in the form of radiation, such as *alpha particles*, *beta particles*, and *photons*. The term may also refer to radioactive materials.

Radioepidemiological Tables: Tables that allow computation of the *probability of causation (PC)* for various cancers associated with a defined exposure to radiation, after accounting for factors such as gender, age at exposure, age at diagnosis, and *time since exposure (TSE)*.

Radon: A radioactive noble-gas element. Radon constitutes a health hazard, primarily to the lungs, when it is released into the air and its decay products are inhaled.

Random seed number: The first number selected in a sequence of random numbers. A given seed value will produce the same sequence of random numbers every time a *Monte Carlo simulation* is run in *NIOSH*-IREP using the same *simulation sample size*.

Relative biological effectiveness (RBE): A mathematical factor used to account for the fact that different types of radiation are more effective at producing an outcome (such as cancer) than others.

Relative risk (RR): The ratio of disease incidence (or mortality) in an exposed population to that in an unexposed population. A relative risk of "1" means there is no association between exposure and disease.

Rem: A unit of measure for expressing *equivalent dose*. One rem is equal to 1 *centi-sievert (cSv)* or 0.01 *sievert (Sv)*.

Risk coefficient: A general term referring to the coefficient of the *dose-response relationship*. In particular, if the dose-response is linear, the risk coefficient is the slope of the dose-response, and it represents the risk of cancer per unit *dose* received by the exposed individual.

Risk model: A mathematical model based on the *dose-response relationship* determined for a given cancer type, used to estimate the *probability of causation (PC)* using information on *radiation dose* and personal data.

SEC: Special Exposure *Cohort*.

Secondary cancer: A cancer that has spread (metastasized) from its site of origin (the primary site) to another part of the body.

SI: The International System of Units

Sievert (Sv): A unit of measure for expressing *equivalent dose*. One sievert (1 Sv) is equal to 100 *rem*.

Simulation sample size: The number of *Monte Carlo simulations* used in each *NIOSH*-IREP run. The default simulation sample size in *NIOSH*-IREP is 2000.

Threshold dose: Radiation dose below which there is no measurable biological effect.

Time since exposure (TSE): The number of years between radiation exposure and diagnosis of cancer.

Uncertainty: A term used to describe the lack of precision and accuracy of a given estimate, the extent of which depends upon the amount and quality of the evidence or data available.

Uncertainty distribution: A range of discrete or continuous values arrayed to encompass, with high confidence, the true but unknown values of a given quantity or parameter.

Upper 99 percent credibility limit: The 99^{th} percentile of the range of values in an *uncertainty distribution*. The *uncertainty distribution* of the *probability of causation (PC)* is first estimated, and the upper 99^{th} percentile of this distribution is compared to the decision criterion (a PC of 50%) to determine eligibility for compensation.

Working Level: A unit of measure describing the level of exposure to radioactive *radon*.

Working Level Month (WLM): A unit of measure describing a cumulative exposure to one *working level* of *radon* for one working month (170 hours.)

X rays: A type of electromagnetic radiation (*photon*) similar to *gamma radiation* but generally less energetic.

7.0 DESCRIPTION OF EXAMPLE INPUT FILES

The input files included on the floppy disk located inside the back cover of this user's guide have been provided to aid Department of Labor (DOL) staff in learning to use NIOSH-IREP. A description of each file is included below. *The simulation sample size has been set to 2,000 and the random seed value has been set to 99 for all example input files.*

Example 1 is included to illustrate how PC is affected by the claimant's age at the time of exposure.

Example 1a

Filename:	Example1a.xls
Gender:	Female
Age at exposure:	20
Age at diagnosis:	50
Cancer type:	Liver
No. of exposures:	1
Exposure rate:	chronic
Radiation type:	high-energy gamma rays (photons; E=30-250 keV)
Dose:	10 cSv (constant)

Example 1a solution

Percentile	Probability of Causation (%)
1st	1.76
5th	3.15
50th	14.16
95th	41.20
99th	53.21

Example 1b

Filename:	Example1b.xls
Gender:	Female
Age at exposure:	40
Age at diagnosis:	50
Cancer type:	Liver
No. of exposures:	1
Exposure rate:	chronic
Radiation type:	high-energy gamma rays (photons; E=30-250 keV)
Dose:	10 cSv (constant)

Example 1b solution

Percentile	Probability of Causation (%)
1st	0.99
5th	1.75
50th	8.34
95th	28.02
99th	39.51

Example 2 is included to illustrate how PC is affected by smoking history.

Example 2a

Filename:	Example2a.xls
Gender:	Male
Age at exposure:	20
Age at diagnosis:	50
Cancer type:	Lung
Smoking history:	Never smoked
No. of exposures:	1
Exposure rate:	chronic
Radiation type:	high-energy gamma rays (photons; E=30-250 keV)
Dose:	Lognormal (geometric mean=15 cSv; geometric sd=2.0)

Example 2a solution

Percentile	Probability of Causation (%)
1st	0.66
5th	1.36
50th	9.15
95th	40.42
99th	57.34

Example 2b

Filename:	Example2b.xls
Gender:	Male
Age at exposure:	20
Age at diagnosis:	50
Cancer type:	Lung
Smoking history:	Smoker (20-39 cigarettes/day)
No. of exposures:	1
Exposure rate:	chronic
Radiation type:	high-energy gamma rays (photons; E=30-250 keV)
Dose:	Lognormal (geometric mean=15 cSv; geometric sd=2.0)

Example 2b solution

Percentile	Probability of Causation (%)
1st	0.22
5th	0.68
50th	4.06
95th	19.21
99th	30.64

Example 3 is included to show how multiple exposures are handled in NIOSH-IREP.

Example 3

Filename:	Example3.xls
Gender:	Male
Age at exposure:	25, 26, 27, 28, 29
Age at diagnosis:	60
Cancer type:	Colon
No. of exposures:	5
Exposure rate:	chronic
Radiation type:	high-energy gamma rays (photons; E>250 keV)
Dose:	Lognormal (geometric mean=5 cSv, geometric sd=1.7)

Example 3 solution

Percentile	Probability of Causation (%)
1st	0.98
5th	3.12
50th	14.19
95th	41.15
99th	56.78

Example 4 demonstrates a calculation for a claimant with 3 radon and 3 other radiation exposures.

Example 4

Filename:	Example4.xls
Gender:	Male
Age at exposure:	20, 21, 22
Age at diagnosis:	50
Cancer type:	Lung
Smoking history:	Never smoked
No. of exposures:	3
Exposure rate:	chronic
Radiation type:	high-energy gamma rays (photons; E>250 keV)
Dose:	Triangular (min=2, mode=4, max=8)
Radon exposure:	Lognormal (geometric mean=0.4 WLM, geometric sd=2)

Example 4 solution

Percentile	Probability of Causation (%)
1st	3.38
5th	5.61
50th	14.79
95th	38.62
99th	53.63